Appeal No. 2013-1454

IN THE UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

PROMEGA CORPORATION,

Plaintiff-Appellee,

v.

APPLIED BIOSYSTEMS, LLC,
LIFE TECHNOLOGIES CORPORATION, and CALIFORNIA INSTITUTE OF TECHNOLOGY,

Defendants-Appellants.

Appeal from the United States District Court
for the Northern District of Illinois,
Case No. 13-CV-2333,
Judge Richard A. Posner.

CORRECTED REPLY BRIEF FOR DEFENDANTS-APPELLANTS

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CERTIFICATE OF INTEREST

Counsel for Defendants-Appellants Life Technologies Corporation, Applied Biosystems, LLC, and California Institute of Technology certifies as follows:

1. The full name of every party or amicus represented by us is:

   Applied Biosystems, LLC
   Life Technologies Corporation
   California Institute of Technology

2. The name of the real party in interest represented by us is:

   Applied Biosystems, LLC
   Life Technologies Corporation
   California Institute of Technology

3. All parent corporations and any public companies that own 10 percent or more of the stock of the parties represented by us are:

   Formerly known as Invitrogen Corporation and traded under the symbol "IVGN," Life Technologies Corporation is a publicly held corporation and is now traded under the symbol "LIFE." Applied Biosystems, LLC is a wholly owned subsidiary of Life Technologies Corporation. When it was formerly part of Applera Corporation, Applied Biosystems was traded under the symbol "ABI."

4. The names of all law firms and the partners or associates that appeared for the parties now represented by us in the trial court or are expected to appear in this Court are:

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PRELIMINARY STATEMENT

Promega's appeal brief confirms that the district court improperly adjudicated this case on summary judgment based on its own legal theories and its own pre-conceived opinions of the facts and technology. The record simply does not support the district court's trial-by-paper approach to this case.

To try to defend the district court's judgment, Promega attempts an improbable about-face from its theory of the case below. It insists that there is double patenting, but it admits it never even pled double patenting, much less did it tender supporting evidence. It insists that there is clear and convincing evidence that U.S. Patent No. 5,118,800 ("Smith '800") anticipates the U.S. Patent No. RE43,096 ("'096 patent"), but its team of experts refused to opine that it anticipates. It insists that the U.S. Patent No. 4,948,882 ("Ruth '882") renders the '096 patent obvious, but Dr. Ruth himself, as Promega's expert, opined that the claims of the '096 patent were not enabled to one of ordinary skill in the art until years after the effective filing date even with the benefit of his patent. It insists that Ruth '882 patent teaches towards the '096 patent, yet at the time of the '096 filing, Dr. Ruth himself (and the research community for that matter) documented a significant concern that the direction pursued by the '096 inventors would not work. Moreover, even Dr. Ruth, although he tried, was not able to use his labeling technology for DNA sequencing despite years of effort. Indeed, Dr. Ruth did not

successfully use his labels for sequencing until 1987, after the '096 inventors' landmark Nature article proving the technology was published in 1986.

A landmark patent was improperly invalidated based on strained theories that are not supported by Promega's trial court positions, much less by the record. The summary judgment rulings should be reversed. Promega's invalidity theories all fail as a matter of law.

ARGUMENT

I. PROMEGA FAILS TO JUSTIFY THE DISTRICT COURT'S USE OF SMITH '800 TO INVALIDATE THE CLAIMS

Promega's invalidity experts included in their lengthy reports a dizzying set of invalidity theories. But, as Promega must concede, its experts did not opine that Smith '800 patent anticipated the claims of '096 patent. And Promega's experts were correct that Smith '800 does not anticipate the claims in suit. Promega's turnaround attempt on appeal to support the district court's conclusion to the contrary fails.

A. SMITH '800 IS NOT PRIOR ART

Analyzing the *Blout, Land,* and *Mathews* line of cases, Life established in its opening brief that an inventor's own work cannot be used as a §102(e) reference against them and that the district court's analysis did exactly that by relying on Smith '800.

Promega does not contest this law. Rather, it makes two arguments why §102(e) does not protect the '096 patent. First, it argues that the sequencing disclosure from Smith '800 used to invalidate the claims-in-suit was *not* invented by the '096 inventors. Second, it argues that the district court's waiver finding prevents Life from proving that Smith '800 is not prior art. Each argument fails and is addressed in turn.

1. THE PORTION OF SMITH '800 RELIED UPON *IS* THE INVENTORS' OWN WORK

As Promega acknowledges, the district court relied only on one sentence from column three and one sentence from column five of Smith '800 relating to DNA sequencing to prove anticipation of the '096 patent. But these two sentences are references to the '096 inventors' own work and thus are not properly prior art. Life Opening Brief at 23-27.

Promega contends that the column three sentence treats DNA sequencing as part of the Smith '800 inventions and refers to the '096 patent as merely teaching the *automation* of DNA sequencing. As an initial matter, the sentence expressly tells you that the information in the sentence is about material in the '096 patent: "As described in the assignees co-pending application [listing the original application in the '096 chain]…." A121. It is improper to use information from the '096 patent as prior art against that patent, but that is exactly what using this sentence does by its express terms.

Moreover, even though all reasonable inferences must favor Life on summary judgment, there is no need for inferences. There is solid, direct evidence that innovations necessary to apply the chemical compounds of the Smith '800 patent to DNA sequencing were invented by the '096 inventors. Application No. 06/570,973 ("'973 application," which matured into the '096 patent) referenced in the column three sentence states that using labeled nucleic acids for DNA sequencing is an invention by the inventors of *that* application. But, even beyond that, Dr. Lloyd Smith himself swore under penalty of perjury that the claims in the '973 application were "joint" inventions "first" invented with his Caltech co-workers listed on the '096 patent – not inventions with his chemistry colleagues listed on Smith '800. A2531.

Specifically, the claims that were the subject of Dr. Smith's inventorship oath with the '096 inventors cover the basic concept of using labeled DNA for sequencing:

> 1. In the method of DNA sequencing by the chain termination method;
> the improvement wherein the primer oligonucleotide is labeled with a colored tag.
>
> 2. In the method of DNA sequencing by the chain termination method;
> the improvement wherein the primer oligonucleotide is labeled with a fluorescent tag.

A6179.

Doctor Smith thus confirms in January 1984 that these broad inventions were *jointly and first* invented with his co-inventors for the '096 patent.[1] This proves that this was *not* the invention of Dr. Smith and the other Smith '800 inventors. A2531.

Promega ignores this compelling evidence. Instead, it attempts to rely upon statements in Application No. 565,010 ("'010 application," which evolved into Smith '800) to suggest that Dr. Smith believed that DNA sequencing was part of his '010 invention, and not the joint work of the '096 inventors, as he had stated in his inventorship oath in support of the '096 patent. Promega Brief at 26. Promega omits important facts. After reviewing who were the true inventors of the innovations in the '010 application, Dr. Smith filed a preliminary amendment, *eliminating* DNA sequencing references from the '010 application because he concluded the sequencing subject matter was unsupportable in the '010 application. A17385-86. Very little remained regarding DNA sequencing when the '010 application was abandoned. And, of course, ultimately in Smith '800 as-issued, there is only the thin column three and column five references to the work in the '096 patent. Put simply, Promega's attempt to rely upon the original references to DNA sequencing in the '010 application decisively favors Life

[1] Professor Smith and the '096 inventorship team again confirmed they together invented the use of labeled DNA for sequencing in their 2003 oath in the '096 file history. A4677-85; *see also* A4892-4906.

because these references were *eliminated* by the applicant as unsupported in Smith '800 and as properly in the '096 applications. *See id.*

Although Promega mentions the column three sentence, it emphasizes the absence of a direct reference to the '096 patent in the column five sentence. But Promega's heavy reliance on the column five sentence ignores that Smith '800 already explained earlier in the disclosure that the DNA sequencing application is the work of the '096 inventorship team. There was obviously no reason to repeat that later in the disclosure in column five.

Promega denies that its own expert acknowledged that the column five sentence is a reference to the DNA sequencing teaching in the '096 patent. But Promega cannot deny that its expert's report states that the column five sentence teaches that the '010 compounds can be used for DNA sequencing, only *if* they have the characteristics "disclosed in the '096 Patent." A11271. That is an undeniable reference to the work of the '096 patent as being indispensable to the application of the Smith '800 labels to DNA sequencing.

The total absence of an enabling disclosure in Smith '800 for the DNA sequencing application, compared to the copious enabling disclosure in the '096 patent itself, should resolve any doubts that the '096 inventors are responsible for the DNA sequencing invention. The reference to their DNA sequencing inventions in Smith '800 by reference to the '096 patent was improperly used to invalidate

that patent. That is never proper, as established by the undisputed legal principles set forth in Life's opening brief, which remain unchallenged.

2. PROMEGA'S WAIVER ARGUMENT FAILS

Promega argues that, even if this Court acknowledges that the supposed anticipatory disclosure in the Smith '800 is indeed the work of the '096 inventors, these inventors' own work should nevertheless be allowed to invalidate their patent under §102(e). Promega's argument fails.

First, Promega never challenges the bedrock §102(e) principle that an "applicant's own invention [], as against them, could not possibly be prior art." *Application of Land*, 368 F.2d 866, 879 (1966). Promega attempts instead to frame the parties' dispute as a garden-variety priority battle regarding proof of an invention date to which the district court's "sanctions" order is applicable.[2] Yet, the *Land* decision acknowledges that, in substance, the §102(e) issue here is properly considered a question of *who* invented the allegedly anticipating disclosure in the putative §102(e) reference, not the date *when* that invention was conceived:

[2] Promega argues that, even if §102(e) did not apply, it would have developed a §102(g) theory. Even assuming that Promega did not pursue a §102(g) theory merely because of its confidence in §102(e), both defenses suffer from the same fundamental problem. The DNA sequencing invention was not conceived by *another*. It was conceived by the '096 inventors (of which Dr. Smith was one), as established on this appeal beyond peradventure.

> We therefore approach the question of the availability of the Land and Rogers '606 patents realistically for what it is, a problem of evidence and a question of fact as to *what disclosure* is relied on in support of the rejection and *who invented* the subject matter disclosed.

Land, 368 F.2d at 878.

Because, realistically, the true issue is a *who* issue, not a *when* issue, the district court's waiver or underlying sanctions ruling should not be used to prevent this Court from recognizing what is apparent from the face of Smith '800. It would elevate form over substance to apply a preclusion order against showing an earlier date of invention to the different and actual question of *who* invented subject matter in a putative §102(e) reference.

Insofar as the district court intended to preclude Life from proving that the disputed material in Smith '800 is the inventors' own work, this would be an abuse of discretion. *Sherrod v. Lingle*, 223 F.3d 605, 612 (7th Cir. 2000). Life's position was substantially justified because preventing an inventors' own work from being used against him or her is different from claiming an earlier date of conception. *Land*, 368 F.2d at 878. Life's interrogatory response was harmless because, as established above, the patent documents themselves conclusively show that Smith '800 was referencing the work of the '096 inventors when it described DNA sequencing. *Id.* at 879 ("When the 102(e) reference patentee . . . had knowledge of the joint applicants' invention by being one of them, and thereafter describes it, he

necessarily files the application after the applicant's invention date"). Promega fails to identify anything that could change the truth that the inventors' own work was improperly used to invalidate their own patent.

In sum, Life should not be prevented from proving *who* invented the subject matter in Smith '800 that is the asserted basis for the district court's anticipation finding.

B. EVEN IF SMITH '800 WERE PRIOR ART, PROMEGA'S ATTEMPT TO DEFEND THE DISTRICT COURT'S INVALIDATION OF CLAIMS FAILS

Promega's attempt to defend the district court's anticipation analysis based on Smith '800 fails. Promega attempts to backfill by introducing an obviousness theory and asking this Court to adjudicate that theory for the first time on appeal. That argument fails too.

1. SMITH '800 DOES NOT ANTICIPATE

In trying to defend the district court's anticipation theory, Promega rewrites history and suggests that it has always thought that Smith '800 anticipates. But the district court flat out acknowledged that "Promega's experts have not said that the '800 patent anticipates the '096 patent." A68. And even though Promega brags that it submitted "more than a dozen expert reports," Promega Brief at 32, it does not identify any anticipation opinion based on Smith '800.

As documented in Life's opening brief, Promega and its experts simply do not believe that the '096 claims are anticipated because they do not even believe that the original '096 application enables the claims. Promega strains to harmonize its conflicting enablement and anticipation positions. Promega contends that its enablement theory relates *only* to the breadth of the claims, but that it believes embodiments of the claims are properly enabled by the original '096 application. This is litigation-driven fiction.

Promega's expert, Dr. Ruth, testified that, even using the entire '096 patent with its incorporation by references of the Smith '800 disclosure in the form of the '010 application, he would *not* be able to replicate the work in that patent. A19097-98. An inability to use a preferred embodiment is hardly a problem of overbreadth. Rather, it is a fundamental issue of whether the technology would work at all or well enough for those of ordinary skill to use it given the relatively primitive state of the art.

The enablement analysis of Promega's other invalidity expert, Dr. Van Ness, was focused on the inadequate length of the primers of the time period. A10243-47. Indeed, Dr. Van Ness opined that, even with the benefit of the Smith '800 disclosure and the '096 disclosure, Dr. Smith was unable to make the inventions of the invalidated claims work in actual practice because he used too short of a primer (12 bases long). A10244-45. Dr. Van Ness suspected this was due to fluorescent

dye's interference with the incorporation of bases using the enzyme, and concluded that some of the disclosed dyes led to smeary results due to the dye's interference with incorporation of bases through the extension process. A10245-46 ("It appears that even months after the 06/570,973 application was filed, a single 12-mer had been tested with only two fluorophores. The attachment of an FITC dye to the 12-mer appears to have resulted in a 'weak' signal, suggesting that the addition of the FITC dye interfered with the hybridization of the 12-mer to the template used in the reaction."). Indeed, Dr. Van Ness did not acknowledge that there were any working embodiments. A10245-46. This too is a fundamental non-enablement position, not a complaint about claim-breadth.

Against this background, Promega's attempt to defend the district court's inherency analysis to fill gaps in the disclosure is fatally flawed. Promega argues that the column three and column five sentences in Smith '800 would explain how to use the compounds for DNA sequencing because it would have been known to select Sanger sequencing – even though Promega's own experts would fear that it would not work and believe that even Dr. Smith could not make it work. However, there were other forms of DNA sequencing such as Maxim-Gilbert and other experimental methods. Indeed, Dr. Ruth failed to use his compounds for DNA sequencing for years based on his documented fear that the large inorganic labels would disrupt the extendibility that is indispensable for Sanger sequencing.

A70 (citing Dr. Ruth Rep. at 19-23); A11663 ¶129. Even the district court acknowledged the trepidation in the community about attempts to extend labeled nucleic acids. A67 ("But fluorescent tags, unlike radioactive ones, might interfere with the chemical reactions in Sanger sequencing.").

Promega places great weight on the testimony of Dr. Smith and Dr. Hood. Promega attempts to interpret Dr. Smith's 2002 testimony that it would be difficult to perform Sanger sequencing without a primer as reflecting the *ordinary* skill in the art *decades* earlier. As a co-inventor, and years after the invention conquered the world of DNA sequencing, Dr. Smith's 2002 knowledge has no probative value on what those of ordinary skill in the art would understand decades earlier when the revolutionary invention was not yet known. Those of ordinary skill had no idea how to use fluorescently labeled nucleic acids for DNA sequencing or extension in the prior art – until the inventions by the '096 inventors transformed the genetics field. In addition, knowing that you can use a primer for Sanger sequencing is different from knowing that use of a primer inherently invoked Sanger sequencing before the invention and that it could be done successfully. Indeed, there is no evidence of that from anyone skilled in the art. Recall that Promega's experts conclude that, even with the rich disclosure of the '973application, one skilled in the art could not make the claimed inventions work.

The only person skilled in the art that addressed whether Smith '800 enables the claims at issue is Life's expert, Dr. Dovichi.[3] He states that the off-hand references to DNA sequencing in Smith '800 do not enable the claimed subject matter. Ironically, even though Promega fails to present *any* expert testimony on this question, even though *it* bears the heavy burden of proving anticipation, and even though it is attempting to rely on two vague sentences to prove that a very important invention was anticipated, it criticizes Dr. Dovichi's enablement opinions for lack of detail. This attempt to shift the burden of proof is unjustified. And Dr. Dovichi's opinion is supported by his extensive analysis of the state of the art. A11637-77. The district court's anticipation ruling should be reversed for this independent reason.

C. SMITH '800 DOES NOT RENDER THE CLAIMS OBVIOUS AND THIS COURT SHOULD NOT ADJUDICATE THAT SUMMARY JUDGMENT ISSUE ON APPEAL

Promega asks this Court to grant its obviousness summary judgment motion in the first instance on appeal as an alternative ground. Further, it asks the Court to extend the ruling to claim 67. The Court should not do so.

[3] Promega's argument that Dr. Ruth opined on this issue by summarily incorporating by reference its invalidity contentions is a credibility loser. Such a reference is, at most, a naked contention, not an opinion. Dr. Ruth did not include an anticipation theory based on Smith '800 in his report.

Promega's obviousness theory is based on its defective anticipation arguments. If the fleeting DNA sequencing references in Smith '800 are not deemed prior art under §102(e) for the good reasons set forth above, Promega's obviousness argument is a nonstarter. But even if they are considered, Promega's position lacks merit.

Promega does not cite expert testimony in support of its obviousness argument based on Smith '800, and it does not acknowledge the skepticism among those of ordinary skill in the art (and Promega's own technical expert) regarding the extendibility of nucleic acids that have large inorganic compounds attached. *See infra*, Section III. Promega also fails to identify why those skilled in the art would create a family of four dyes to work together when neither Dr. Ruth, nor any other prior art, teaches this. As noted in the prior section, Promega does not even believe the '096 inventors were able to achieve this in practice for years after they submitted their application.

Promega also fails to analyze the secondary considerations of non-obviousness. *See Ruiz v. AB Chance Co.*, 234 F.3d 654, 667 (Fed. Cir. 2000) ("The district court erred in failing to consider, or at least to discuss, evidence of secondary considerations. Our precedents clearly hold that secondary considerations, when present, must be considered in determining obviousness."). It is undisputed that "the ['096] inventors made a breakthrough in biochemistry by

developing a way to attach a fluorescent tag to a DNA strand without preventing that strand from extending during replication." A36. Before the '096 patent, there was no known way "to extend a fluorescently tagged DNA strand and thus enable the use of fluorescent tagging in any method of nucleic acid sequence analysis, including DNA sequencing." A36-37. Prior art methods used radioactive labels, "but these were expensive, required costly safety precautions, and could not be read reliably by a computer." A67. The '096 invention not only solved expense and safety problems, but it enabled much more efficient genetic analysis. A96 (5:51-60); *see also* A72 ("If you had 100,000 fragments that you'd like to map, being able to multi-plex and have a quarter as many measurement reactions for them would be very attractive.").

As a result, the invention "revolutionized molecular biology." A19599:16-18. The invention "enabled the human genome project, which is probably the most transformational big science project in all of biology." A19599:20-22. As the district court recognized, "no one disputes that the ['096] invention gained widespread use in the genetic analysis industry" and is considered "a major DNA invention." A39-40. The invention is "important and necessary technology for the industry." A12565. There are no commercially viable alternatives. A12565-66. Promega's own marketing efforts highlight the patented technology. A12564; A32-36; A12577; A1476 ¶75. Inventor Dr. Leroy Hood received numerous

awards for the technology, including the Kyoto Prize, induction into the Inventors Hall of Fame, the Russ Prize, and the National Medal of Science. A19600:4-7; A19601:17-19602:11. Thus, secondary considerations of skepticism, praise, and commercial success all point towards the nonobviousness of the invention. In finding claim 67 obvious, the district court discussed only the opinion of one expert Dr. Dovichi. A72-73. During the rushed summary judgment process, the district court failed to consider the above evidence, including the court's own prior findings acknowledging the revolutionary nature of the invention.

II. PROMEGA FAILS TO JUSTIFY THE DISTRICT COURT'S USE OF THE SMITH '800 SPECIFICATION FOR OBVIOUSNESS-TYPE DOUBLE PATENTING

Promega does not deny that the district court used the specification of Smith '800 for its obviousness-type double patenting analysis. Promega does not deny that the district court needed to rely upon the specification to find double patenting. Promega does not deny that as a general rule, the specification should *not* be used for such an analysis.

Promega attempts to rely upon a "limited exception" to the rule that only claims should be considered in double patenting analyses. This exception allows the earlier patent's *specification* to be considered as part of the prior art under very limited circumstances. As explained in Life's opening brief, Promega attempts to balloon the limited *Lilly* exception until it overruns venerable authority such as Judge Rich's decision in *In Re Kaplan*, 789 F.2d 1574 (Fed. Cir. 1986). *Kaplan* is

on all fours with this case because, as here, it involves an earlier patent that discloses the work of the inventors of the later patent because of an overlap of inventorship. The limited *Lilly* exception may allow reference to the specification of the earlier patent, but it does not allow the use of inventors' own work as reported in that specification against them.

To try to avoid the import of *Kaplan*, Promega makes only one lonely and unpersuasive distinction. Promega Brief at 54-55. Promega argues that *Kaplan* does not apply because the earlier patent includes process claims and is not "directed to compounds." *Id.* Promega does not explain why the form of the earlier claim would or should matter in determining whether the specification can be treated as part of the prior art. In Kaplan, the claim stated that "the reaction is effected in the presence of an organic solvent." *In re Kaplan*, 789 F.2d at 1575. Although the claim is nominally a process, what mattered for prior art purposes was the presence of a compound – an organic solvent. Indeed, in its rejection, the Patent Office "relied on the fact that claim 4 calls for 'an organic solvent,'" not that it was a process claim. *Id.* at 1580. The earlier claim at issue in *Kaplan* is, thus, effectively directed to a compound.

In any event, in *Kaplan*, the Federal Circuit rejected the Patent Office's attempt to use the specification of the earlier patent as prior art because it referred

to the invention of the later patent and thus should not be used as prior art at all, not because of the claim form:

> In effect, what the board did was to use a disclosure of appellants' own joint invention which had been incorporated in the Kaplan sole disclosure to show that their invention was but an obvious variation of Kaplan's claimed invention. That amounts to using an applicant's invention disclosure, which is not a 1-year time bar, as prior art against him. That is impermissible.

Id. (citation omitted). Promega totally fails to address this critical reasoning of *Kaplan.* Promega's lone distinction based on the "process" format of the *Kaplan* claim bears no relationship to the rationale of Judge Rich's decision and is thus meaningless.

Promega also contends that who invented the subject matter in the specification of an earlier patent is never relevant to double patenting. For this, Promega cites *In re Hubbell*, 709 F.3d 1140, 1148 (Fed. Cir. 2013). But *Hubbell* sheds no light at all. There, the general rule that obviousness-type double patenting strictly involves a comparison of only *claims* was respected. Life has not contended that the comparison of claims is limited to claims of identical inventorship. Rather, Life has explained that, under *Kaplan*, one may not rely on an inventor's own work to invalidate a subsequent patent when that work is being reported in the *specification of* an earlier patent. Promega's attempt to expand the very limited *Lilly* exception should be rejected. *Kaplan* proves that the

inventorship of the unclaimed disclosure in the earlier patent not only matters, but is dispositive.

Finally, Promega ties itself in knots defending the district court's introduction of the double patenting issue in the case. There is no legitimate defense for the distorted procedure followed here, which effectively repositions the Court as a combatant. Regardless, Promega's failure to itself plead obviousness-type double patenting is best explained by the lack of merit of the position. Although Promega now contends that double patenting is apparent, its conduct during the years of litigation shouts to the contrary.

III. RUTH '882 PROVES *NON*-OBVIOUSNESS, NOT OBVIOUSNESS

Although the district court found that only (and improperly) claim 67 was rendered obvious based on Ruth '882, Promega asks this Court to find that all asserted claims are obvious in the first instance on appeal. But Ruth '882 teaches away, not towards the '096 inventions, as demonstrated below.

Promega attempts to rewrite the history of the breakthrough through invention at issue in this case. The '096 technology moved the world from the crude and dangerous radioactive technology in routine use at the time to a new era of high-speed and high quality DNA analysis using fluorescent labeling.

Although researchers were trying to apply fluorescence technology to nucleic acids for years, and the desire to eliminate radioactivity in DNA analysis

was ubiquitous, no one was able to devise a successful approach before the '096 inventors. The conventional wisdom taught *against* the use of fluorescent labels to extend DNA for sequencing and *against* the use of multiple labels. *Standard Oil Co. v. American Cyanamid Co.*, 774 F.2d 448, 454 (Fed. Cir. 1985) ("A person of ordinary skill in the art is also presumed to be one who thinks along the line of conventional wisdom in the art and is not one who undertakes to innovate, whether by patient, and often expensive, systematic research or by extraordinary insights, it makes no difference which.").

Although Promega contends Dr. Ruth's work renders the '096 claims invalid, it does not deny that, even though Dr. Ruth first synthesized a fluorescent oligonucleotide in June 1982 and was interested in DNA sequencing, it took him until *1987* to finally extend his oligonucleotides for DNA sequencing. *See* A11661 ¶124. And Dr. Ruth's success was only *after* the '096 inventors' landmark Nature article announced the breakthrough to the world. A13269-74.

Promega does not dispute that the district court recognized that Dr. Ruth and the community believed that "fluorescent tags, unlike radioactive ones, might interfere with the chemical reactions in Sanger sequencing." A67; *see also* A70 ("Many prior art references—such as Ruth '882 patent, the application for which was filed in February 1983—explained how to attach fluorescent tags to

oligonucleotides, even though it was uncertain whether the resulting oligonucleotides could always be extended.").

Dr. Ruth expressed his fears to the whole community. In the Ruth '882 patent, he cautioned readers about "the interference of the modifications [such as labeling] with the activity of the enzymes." A11663 ¶129. Life's expert explained that the bulky, inorganic labels used by Dr. Ruth would have discouraged those skilled in the art from pursuing the extension of fluorescent labeled oligonucleotides. *See, e.g.*, A11663-67 ¶130 ("A person with ordinary skill [in the art] would have expected the very large and bulky modification proposed by Ruth to destabilize hybridization between the modified oligonucleotide and its complement, and that destabilization would have interfered with any chain extension reaction involving the modified oligonucleotide.").

This is consistent with Dr. Ruth and Dr. Van Ness' expert opinions, addressed above, that, given the state of the art, they believed persons skilled in the art would not even be able to successfully use the embodiments in the '096 patent with the full '096 disclosure. Regarding claims 62 and 66 (and their dependents) Promega nevertheless asserts that "Ruth '882 explicitly taught that oligonucleotides can be modified so as to not interfere with polymerase." Promega Brief at 61. For this, Promega relies on the passages in Ruth referenced above, and relied upon by the district court, in which Dr. Ruth expresses his fears about the

"interference" the modifications will have to extension. Promega argues that, if labeled oligonucleotides can hybridize to a target, they necessarily can extend for DNA sequencing. Promega Brief at 62. This attorney surmise conflicts with the detailed and persuasive testimony of Dr. Dovichi to the contrary and with Promega's own experts' enablement opinions, the district court's conclusions, and Dr. Ruth's and the scientific communities' fears of failure, and even Dr. Ruth's multi-year failed effort to do what Promega now argues was obvious.

Regarding claim 67, the only claim the district court found obvious based on the Ruth patent, Promega's arguments are so weak that, not only should summary judgment be vacated, but this obviousness theory should be eliminated as a matter of law. Promega's experts opined that the '096 patent itself does not provide sufficient information to allow a person skilled in the art to use four working dyes and oligonucleotides that are long enough to function.[4] Yet Promega contends that Ruth's generic laundry list of potential labels is sufficient to allow an ordinary person skilled in the art to develop a family of four working labels. Promega Brief at 63 (citing Ruth at 7:63-8:4.).

Given the science, and the views of Promega's experts about how difficult it is to find working dyes, Promega's position strains credulity. Promega relies

[4] Promega's insistence that its enablement arguments relate only to single lane sequencing embodiments finds no support in the record. *See supra*.

heavily on the statement from Life's technical expert that, if there was an issue with one of the dyes disclosed in the '973 application (to which the '096 patent claims priority), it would have been straightforward to substitute another. But this statement is in the context of the '973 application, which has a rich set of disclosures regarding the labeling of oligonucleotides to create a family of four dyes. Dr. Ruth and the scientific community were afraid of extension in the presence of large, inorganic labels and even Dr. Ruth did not accomplish DNA sequencing until years later. He was not able to put together a family of four dye labeled oligonucleotides for DNA sequencing.

Promega does little to defend the district court's unsupported conclusion that one skilled in the art would be motivated to, and could, create or locate a family of four dyes for DNA sequencing when they were not even confident they could make one extendible oligonucleotide that is labeled with inorganic dyes. Life's detailed explanation of why the district court's technical analysis is wrong has not been meaningfully rebutted. Life Opening Brief at 47-50.

In addition, as explained above at Section I.C, the potent secondary considerations of non-obviousness for this revolutionary invention preclude a finding of obviousness as a matter of law.

IV. PROMEGA'S RESPONSE CONFIRMS THAT THE DISTRICT COURT IMPROPERLY FOUND A WRITTEN DESCRIPTION VIOLATION

The district court's written description analysis for claim 62 and dependents includes essentially one sentence of analysis. A77. That sentence reasons that, instead of Sanger sequencing, the accused products use the claimed methods with PCR, which had not been invented at the time of the '096 invention. *Id.*

Promega argues that, any time there are two embodiments within the scope of a claim, it is a genus claim that must be strictly scrutinized for a written description violation. This makes no sense. Virtually every claim can be said to have multiple embodiments. Promega's argument is empty.

The claimed methods are extendible oligonucleotides with novel labels. Promega has not identified any meaningful difference between extending olignuclotides for Sanger sequencing and doing so for PCR. In all relevant ways, the inventions work the same way. Even though Promega bears the burden of proving invalidity with clear and convincing evidence, it does not identify any expert testimony that could support the district court. Indeed, it does not even argue that the claimed inventions work differently with PCR than they do with Sanger sequencing.

There is no written description violation. Promega's view of the law would punish revolutionary inventions such as this one by creating an unattainable

prescience about how the breakthrough might be applied in the future. This defense should be eliminated as a matter of law.

V. THE EXCLUSION OF LIFE'S DAMAGES EXPERT WAS CONTRARY TO WELL-SETTLED DAMAGES LAW

As shown in Life's opening brief, the district court erred by excluding the reasonable royalty testimony of Life's damages expert Greene. The district court based its decision on a fundamental factual error (an erroneous belief that Greene did not analyze comparable licenses), on a newfound requirement that Greene conduct a type of lost profits analysis as a precondition to a reasonable royalty analysis, and on an impossible standard for precise quantification directly contrary to *Georgia-Pacific*. Life Opening Brief at 57-60.

To attempt to defend the district court's elimination of Life's damages opinion, Promega argues that in analyzing a 2012 hypothetical negotiation, Greene improperly "discarded" a 2% rate from the parties' 2006 Cross License and "did not analyze" other licenses he relied upon. Promega Brief at 67, 70.

Promega's argument relies entirely on a false premise. Promega asserts that "there are no changed circumstances between 2006 and the time of reissue" in 2012. Promega Brief at 68. Promega provides no support for this assertion. *Id.* (citing no evidence). In fact, Greene analyzed several important changed circumstances between 2006 and 2012 that justified a higher royalty rate in 2012:

- The 2% rate was a sweetheart deal made when Life was on the ropes. As Greene explains, "Life also had very little negotiation power to ask for a higher rate. . . . Life was negotiating as the Defendant in a lawsuit brought by Promega in 2001." A12562. *Promega* admitted that the royalty rate in the 2006 Agreement was "not comparable to the rate that would apply in an arms length negotiation" because the 2006 Agreement "was a specialized circumstance, settling longstanding disputes." A12562; *see also* A11857 ("The 2006 agreements included a cross-license that had a significant number of other terms and considerations that would not be included in the hypothetical license, including . . .").

- The unlicensed fields have become increasingly important commercially since 2006. "After the agreement was executed in 2006, an unexpected increase in demand of the accused products occurred." A11855. "By 2012, the forensic and paternity use of STR kits had grown substantially, the use of STR kits in fields outside of the Genetic Identity Field of use expanded, and Promega was selling qPCR products." *Id.* In 2012, "fields outside the scope of the agreement" were growing and had high hopes for these markets. A12562-64; *see also* A11832 (double digit growth for Life from 2004 to 2011); A11857-58.

- The '096 patent came out of reissue in 2012 stronger than Promega expected. A11853; A11856. "The '096 patent is [] broader than the original '748 patent." A11856. Contrary to Promega's assertion, the only relevant consideration is not "if and when the patent did reissue." Promega Brief at 68. The broader *scope* of the reissued patent would also have been important to the parties' negotiation. That is because "core patents generally drive a higher royalty rate." A12565.

Thus, Greene persuasively explained why the 2% rate in the 2006 Cross License would not have been adopted by the parties in 2012. Promega's contention that Greene erred by "discarding" the 2% rate because "there are no changed circumstances between 2006" and 2012 is entirely unsupported. Promega Brief at 68; A50 (district court faulting Greene for similar reasons).

Promega and the district court ignore persuasive evidence, presented by Greene, showing that customary licensing rates for core patents in the field were 11-12%, and as high as 30-40%. The '096 is such a core patent:

- Promega admitted that "royalty rates of 11 to 12 percent" are appropriate for "core patents for STR analysis." A12565. The '096 patent "covers a central function of STR and qPCR products" and "has the characteristics of what [Promega's Chief Technology Officer and expert witness] Dr. Dimond describes as a 'core' technology." A12566 "Dr. Dimond also concluded in his expert report regarding damages that reasonable royalty for the fields not previously licensed to Life would be no less than 12%." A11840. Use of potentially alternative technologies "would likely exceed the cost of the royalty determined in this report." A11849.

- For a hypothetical negotiation where the licensor does not want to license the technology, a 35-40% royalty might be "expect[ed]" due to the high profit margins in the industry. A11838-39. Promega's profitability is over 70%. A11839. Promega "had previously paid as high as a 30% royalty for earlier forensic and paternity technology." A11840.

- "Promega and Life essentially represent the entire market for supplying STR kits." A11845. Promega's Chief Technology Officer testified that "if one of the companies was no longer selling to that market, [customers] would simply go to the other source[.]" A11903. These factors "would have an upward effect on the determination of a royalty in this matter." A11904.

- "Promega has paid an effective royalty of 13.3% on the accused products since March 2001." A11915. "In 2012, Promega paid royalty expenses of 12.1% and 6.1% for STR and qPCR products, respectively." *Id.*

The above evidence shows that Greene's 10% rate is reasonable. This is only a fraction of the evidence he considered. *See generally* A12574-76

(summarizing). Promega ignores all this evidence of customary rates in the industry in its quest to hold Life/Caltech to a sweetheart deal negotiated in 2006 when Life was on the ropes. The district court did the same based on the false premise that the 2006 rate was somehow a necessary starting point, any deviations from which had to be precisely quantified, on pain of having all expert testimony stricken. That was error.

The blanket assertion that Greene "did not analyze" the licenses he relied upon is simply false. Promega Brief at 70; A50. Greene's detailed analysis of the USB, Amersham, Shimadzu, Visible Genetics, Kit Manufacturing Licenses, Probe Manufacture Agreements, and other licenses occupies 41 pages of his opening report and 8 pages of his supplemental report, including:

- For each license, Greene analyzed its scope and financial terms, the licensed technology, the products at issue, the economic circumstances underlying the agreement including considerations related to royalty stacking and relationship between licensor and licensee, the license term, and other factors. *See generally* A11860-11901; A12565-74.

- For comparable licenses Greene relied on, Greene concluded that "[t]he licensed technology is similar," "[p]roducts incorporating the patented technology are similar to the accused products," and the "[l]icensor is the same." *See, e.g.*, A11862-63, A11866-67, A11871.

- For licenses that Greene did not rely on, Greene concluded that the products at issue (e.g., medical instruments) are significantly different than the accused products in terms of cost and profit margin, the technology is not comparable, or the original agreement is not available and so its comparability to the hypothetical negotiation

> cannot be determined. *See, e.g.*, A11868, A11876, A11892, A11894, A11897.

Finally, as stated in Life's opening brief, the district court improperly impugned Greene for allegedly not being able to identify the licenses he relied on at the *Daubert* hearing. A50. That is as untrue as it is irrelevant. Greene was only asked to "pick one license" to describe as an example. A18077:6-18078:10 (identifying Amersham license). Nothing in his testimony disowned his report, or suggested it should not be considered as the complete basis of his opinions. *See* Fed. R. Civ. P. 26(a)(2)(B)(i). Promega does not defend the district court's error on this point.

The district court's order striking Life's damages report should be reversed.

CONCLUSION

The Court should reverse the district court's judgment below in accordance with the relief requested above.

Dated: November 12, 2013

Respectfully submitted,

By /s/ *Edward R. Reines*

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CERTIFICATE OF COMPLIANCE

The undersigned certifies that this brief complies with the type-volume limitations of Fed. R. App. P. 32(a)(7)((B). This brief contains 6,671 words as calculated by the "Word Count" feature of Microsoft Word 2010, the word processing program used to create it.

The undersigned further certifies that this brief complies with the typeface requirements of Fed. R. App. P. 32(a)(5) and the type style requirements of Fed. R. App. P. 32(a)(6). This brief has been prepared in a proportionally spaced typeface using Microsoft Word 2010 in Times New Roman 14 point font.

Dated: November 12, 2013

/s/ Edward R. Reines

Edward R. Reines

Counsel for Defendants-Appellants

CERTIFICATE OF SERVICE

In accordance with Fed. R. App. P. 25 and Fed. Cir. R. 25, I certify that on this 14th day of November, 2013, I served the foregoing via the Court's CM/ECF system on the principal attorneys for each party.

Dated: November 14, 2013

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